WE CLAIM:

1. A method of generating angiostatin *in vitro* comprising contacting plasminogen with a plasminogen activator and a sulfhydryl donor.

2. The method of Claim 1 wherein the plasminogen activator is selected from the group consisting of urokinase, streptokinase, and tissue plasminogen activator.

3. The method of Claim 1 wherein the sulfhydryl donor is selected from the group consisting of cysteine, N-acetyl cysteine, captopril, D-penicillamine, and reduced glutathione.

4. The method of Claim 1 wherein the angiostatin is at least partially purified from the reaction mixture.

5. The method of Claim 1 further comprising administering an effective amount of the angiostatin to an animal in need thereof.

6. The method of Claim 4 further comprising administering an effective amount of the angiostatin to an animal in need thereof.

7. A method of generating angiostatin *in vitro* comprising:

contacting plasminogen with a plasminogen activator to produce plasmin; and

contacting the plasmin with a sulfhydryl donor to produce the angiostatin.

8. The method of Claim 7 wherein the plasminogen activator is selected from the group consisting of urokinase, streptokinase, and tissue plasminogen activator.

9. The method of Claim 7 wherein the sulfhydryl donor is selected from the group consisting of cysteine, N-acetyl cysteine, captopril, D-penicillamine, and reduced glutathione.

10. The method of Claim 7 wherein the plasmin is at least partially purified prior to contacting it with the sulfhydryl donor.

11. The method of Claim 7 wherein the angiostatin is at least partially purified from the reaction mixture.

12. The method of Claim 7 further comprising administering an effective amount of the angiostatin to an animal in need thereof.

13. The method of Claim 11 further comprising administering an effective amount of the angiostatin to an animal in need thereof.

14. A method of generating angiostatin *in vitro* comprising contacting plasmin with a sulfhydryl donor.

15. The method of Claim 14 wherein the sulfhydryl donor is selected from the group consisting of cysteine, N-acetyl cysteine, captopril, D-penicillamine, and reduced glutathione.

16. The method of Claim 14 wherein the angiostatin is at least partially purified from the reaction mixture.

17. The method of Claim 14 further comprising administering an effective amount of the angiostatin to an animal in need thereof.

18. The method of Claim 16 further comprising administering an effective amount of the angiostatin to an animal in need thereof.

19. A method of treating an angiogenic disease comprising administering to an animal suffering from such a disease an amount of a sulfhydryl donor effective to cause the conversion plasmin to angiostatin.

20. The method of Claim 19 wherein the sulfhydryl donor is selected from the group consisting of cysteine, N-acetyl cysteine, captopril, D-penicillamine and reduced glutathione.

21. The method of Claim 19 wherein an effective amount of plasmin is also administered to the animal.

22. The method of Claim 19 further comprising administering an effective amount of a plasminogen activator to the animal to convert plasminogen to plasmin.

23. The method of Claim 22 wherein the plasminogen activator is selected from the group consisting of urokinase, streptokinase and tissue plasminogen activator.

24. The method of Claim 22 wherein an effective amount of plasminogen is also administered to the animal.

25. A composition for generating angiostatin comprising a sulfhydryl donor and a plasminogen activator.

26. The composition of Claim 25 wherein the sulfhydryl donor is selected from the group consisting of cysteine, N-acetyl cysteine, captopril, D-penicillamine and reduced glutathione.

27. The composition of Claim 25 wherein the plasminogen activator is selected from the group consisting of urokinase, streptokinase and tissue plasminogen activator.

28. The composition of Claim 25 which is a conditioned culture medium produced by culturing cells capable of producing plasminogen activator in a culture medium or is a lysate of such cells.

29. A container holding a plasminogen activator, said container having a label thereon instructing administration of the plasminogen activator to an animal suffering from an angiogenic disease.

30. The container of Claim 29 further holding a sulfhydryl donor and said label on said container instructing administration of the combination of the sulfhydryl donor and plasminogen activator to an animal suffering from an angiogenic disease.

31. A container holding a sulfhydryl donor, said container having a label thereon instructing administration of the sulfhydryl donor to an animal suffering from an angiogenic disease in an amount effective to cause conversion of plasmin to angiostatin.

32. A method of generating angiostatin comprising:

culturing cells capable of producing plasminogen activator in a culture medium for a time sufficient to produce conditioned culture medium (CCM) capable of converting plasminogen into angiostatin; and

contacting the CCM with plasminogen to produce the angiostatin.

33. The method of Claim 32 wherein the cells are selected from the group consisting of cancer cells, primary endothelial cells, smooth muscle cells and fibroblasts.

34. The method of Claim 32 wherein the angiostatin is at least partially purified from the CCM.

35. The method of Claim 32 further comprising administering the angiostatin to an animal in need thereof.

36. The method of Claim 34 further comprising administering the angiostatin to an animal in need thereof.

37. A method of generating angiostatin comprising:

culturing and thereafter lysing cells capable of producing plasminogen activator; and

contacting the lysate with plasminogen to produce the angiostatin.

38. A protein having the following characteristics:

(a) it is a fragment of plasminogen;

(b) its N-terminal amino acid is the same as the N-terminal amino acid of plasmin;

(c) its C-terminal amino acid is in kringle 5; and

(d) it inhibits angiogenesis.

39. The protein of Claim 38 which comprises at least 50% of kringle 5.

40. The protein of Claim 39 which comprises at least 75% of kringle 5.

41. The protein of Claim 38 which is a fragment of human plasminogen and which has the following additional characteristic:

(e) it has an approximate molecular weight of 50-60 kD on polyacrylamide gel electropheresis under non-reducing conditions.

42. The protein of Claim 41 having the following additional characteristics:

(f) it has the N-terminal sequence:

Lys Val Tyr Leu Ser Glu Cys Lys Thr Gly

[SEQ ID NO:1]; and

(g) it has the C-terminal sequence:

Cys Tyr Thr Thr Asn Pro Arg [SEQ ID NO:4]; or

Cys Tyr Thr Thr Asn Pro Arg Lys [SEQ ID NO:5].

43. A DNA molecule comprising a sequence which codes for the protein of any one of Claims 38-42.

44. The DNA molecule of Claim 43 wherein the coding sequence is operatively linked to expression control sequences.

45. A host cell comprising the DNA molecule of Claim 44.

46. A method of producing a plasminogen fragment which inhibits angiogenesis comprising culturing the host cell of Claim 45.

47. An antibody which binds selectively to native angiostatin.

48. A method of detecting or quantitating native angiostatin in a material suspected of containing native angiostatin, the method comprising:

contacting the material with the antibody of Claim 47; and

detecting or quantitating any native angiostatin present in the material.

49. A kit for detecting or quantitating native angiostatin comprising a container holding the antibody of Claim 47.

50. An antibody which binds selectively to the protein of Claim 38.

51. A method of purifying a protein of Claim 38 from a material containing it, the method comprising:

contacting the material with the antibody of Claim 50 so that the antibody binds to the protein; and

separating the protein bound to the antibody from the remainder of the material.

52. A method of treating an angiogenic disease comprising administering to an animal suffering from such a disease an effective amount of the protein of any one of Claims 38-42.

53. The method of Claim 52 wherein the protein is native angiostatin.

54. A method of treating an angiogenic disease comprising administering to an animal suffering from such a disease a transgene comprising DNA coding for the protein of Claim 38 operatively linked to expression control sequences.

55. The method of Claim 54 wherein the protein coded for by the transgene is native angiostatin.

56. A method of treating an angiogenic disease comprising administering to an animal suffering from such a disease an amount of a plasminogen activator effective to cause the conversion plasminogen to plasmin.

57. The method of Claim 56 wherein an effective amount of plasminogen is also administered to the animal.

58. The method of Claim 56 wherein the plasminogen activator is selected from the group consisting of urokinase, streptokinase and tissue plasminogen activator.